This Page Is Inserted by IFW Operations and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

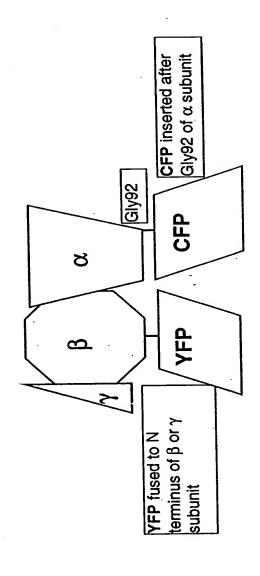
Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.

G Protein Biosensor



Activation/deactivation of G protein Biosensor in Biosensor Cell provides FRET Signal Response

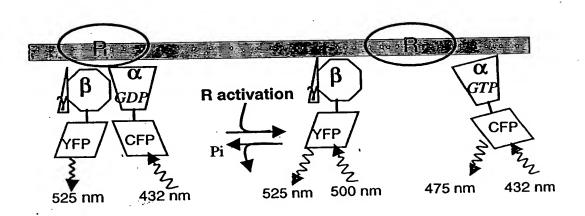
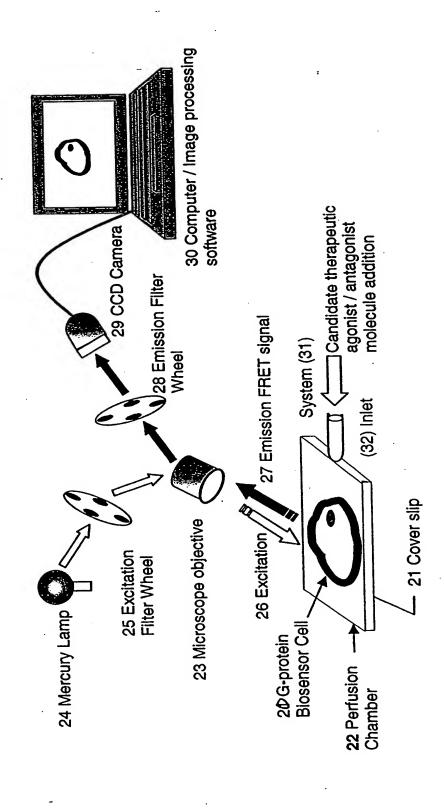


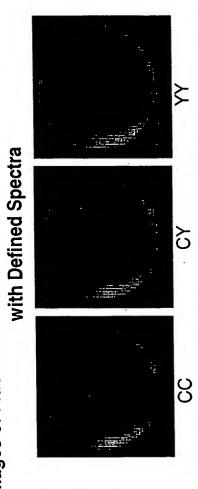
Fig. 2

Fig. 3

Operation of G Protein Biosensor Cell



Images of Fluorescence Emission from Biosensor Cells excited with Defined Spectra



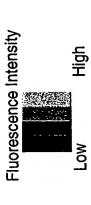


Fig.

Biosensor Cell responds to addition of Agonist drug Carbachol with reduction in FRET Signal Intensity

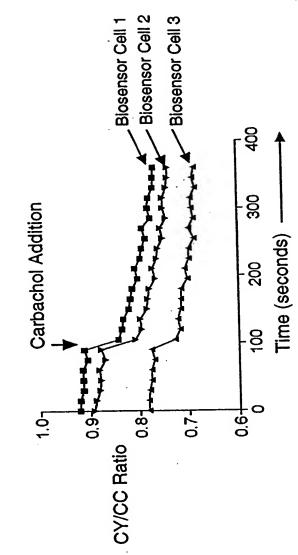


Fig. (

Biosensor Cell responds to increasing concentrations of Agonist

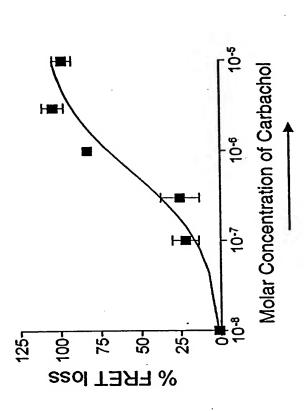
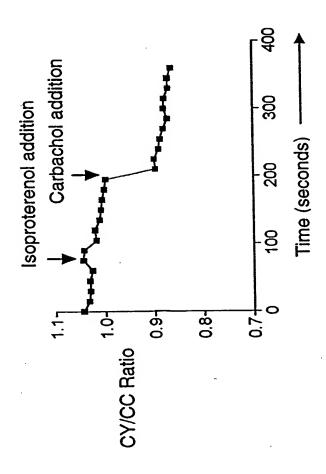


Fig. 7

Biosensor Cell does not respond to unrelated drug Isoproterenol



Biosensor Cell response to Agonist drug action is inhibited by Antagonist drug

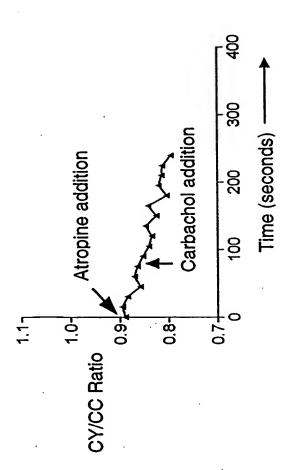


Fig. 9

Biosensor Cell responds to sequential addition of Agonist and Antagonist with predicted changes in FRET Signal Intensity

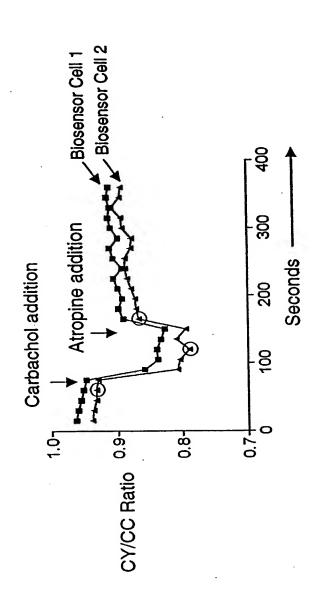
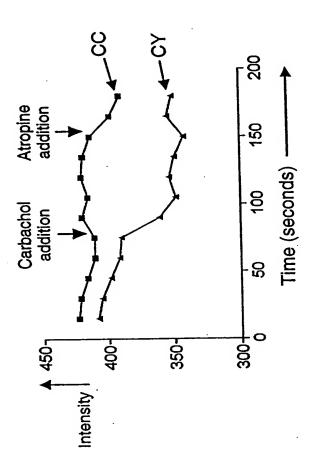


Fig. 10

Biosensor Cells respond to Agonist drug and Antagonist drug with predicted changes in CC and CY emissions



FRET Signal Intensity is Reduced in Parts of Biosensor Cell by Agonist Drug and Increased by Antagonist Drug

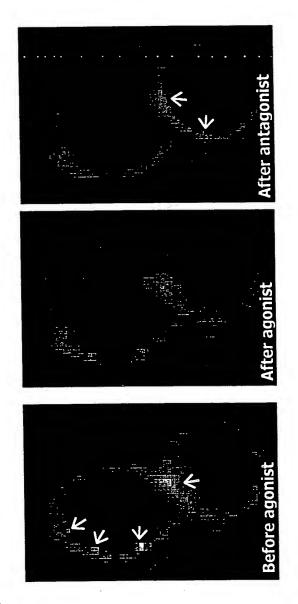




Fig. 12

Biosensor Cell responds to addition of Agonist Neurotransmitter Serotonin with decrease in FRET Signal Intensity

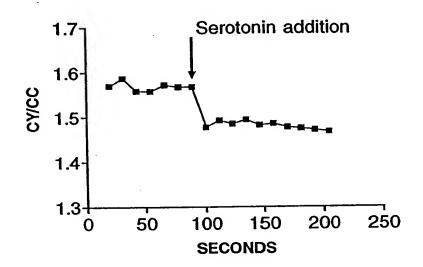


Fig. 13

Biosensor Cell responds to addition of Agonist with decrease and to Antagonist drug with increase in FRET Signal Intensity

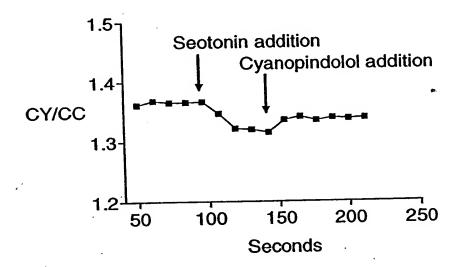


Fig. 14

Biosensor Cell responds to addition of Agonist Drug Adenosine N6-Cyclohexyl. with decrease in FRET Signal Intensity

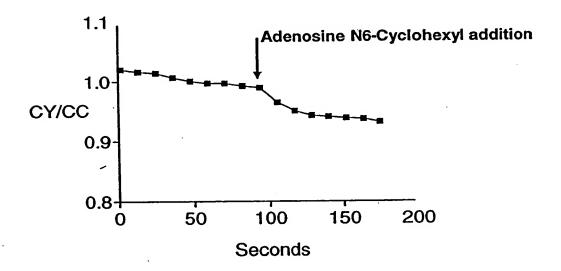


Fig. 15

Biosensor Insect Cell responds to addition of Agonist Drug Carbachol with decrease in FRET Signal Intensity

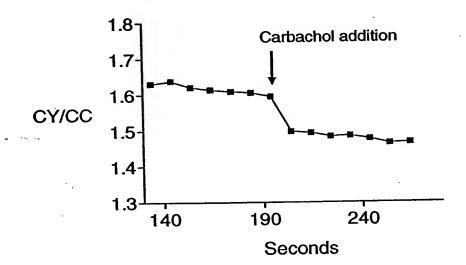


Fig. 16

Biosensor cells containing $\alpha\text{-CFP}$ β $\gamma\text{-YFP}$ respond as predicted to addition of Agonist drug Carbachol

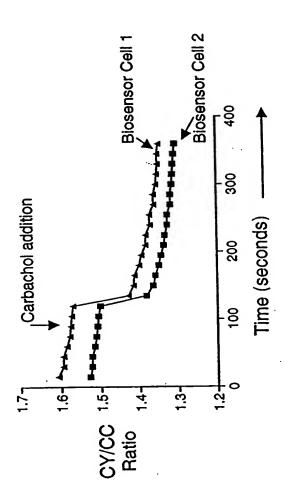
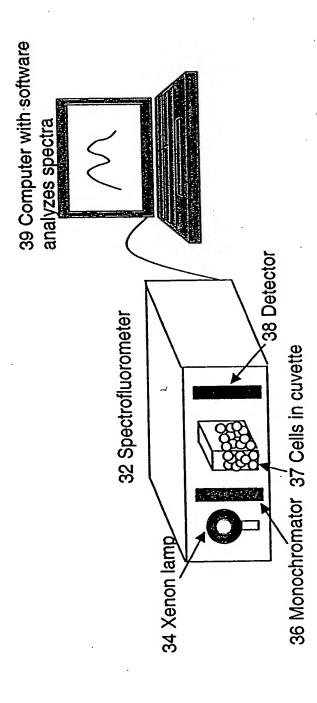
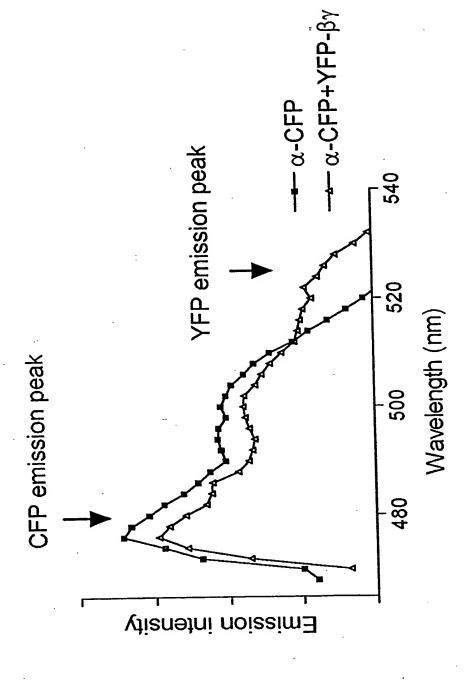


Fig. 17

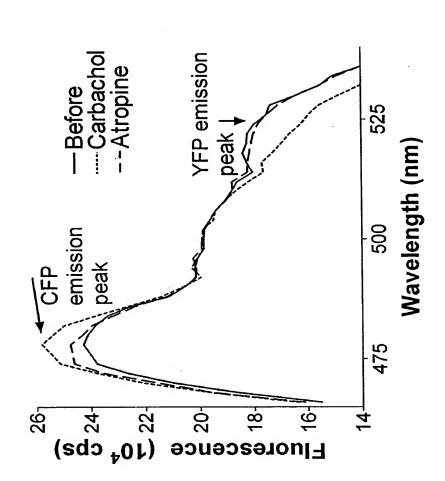
Operation of G protein Biosensor Cell



Fluorometric spectra from Biosensor cells and cells expressing biosensor component proteins

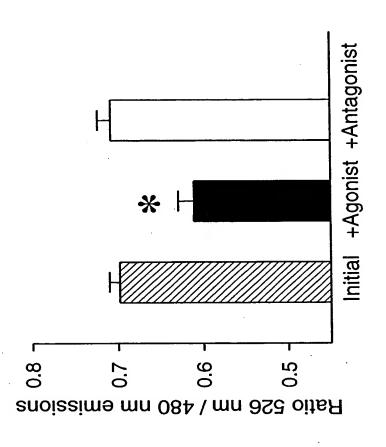


Spectra from Biosensor cells excited at 433 nm after exposure first to Agonist and then Antagonist



Fluorometric measurement of Biosensor cell response to agonist and antagonist

Fig. 20



* Significant (p<0.05)

Fluorometric spectra from Biosensor cells excited at 485 nm

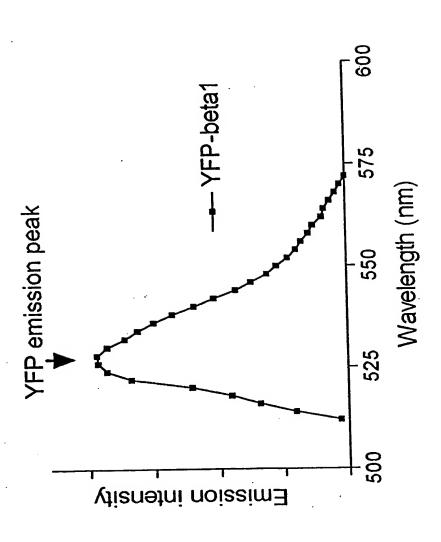
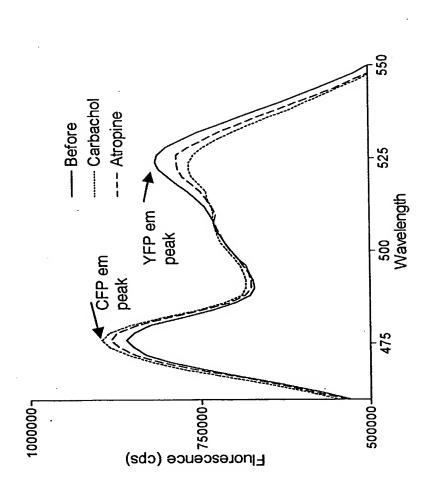
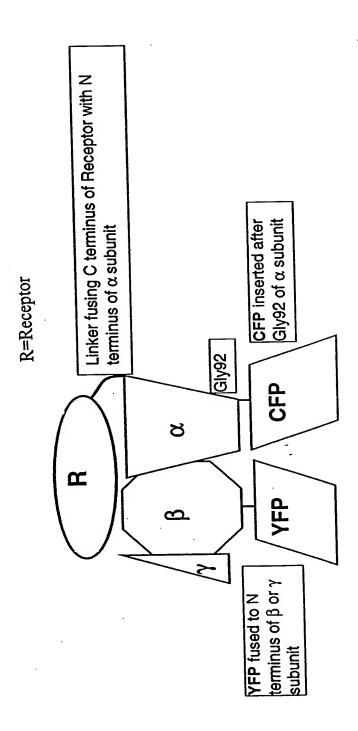


Fig. 22

Spectra from G protein Biosensor Insect Cells excited at 433 nm in response to addition of Agonist and Antagonist



Receptor-G protein sensor



Control of the contro



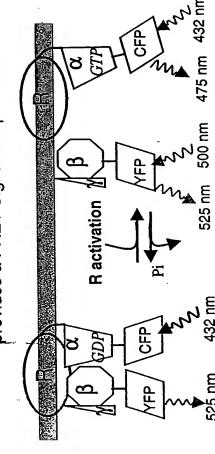
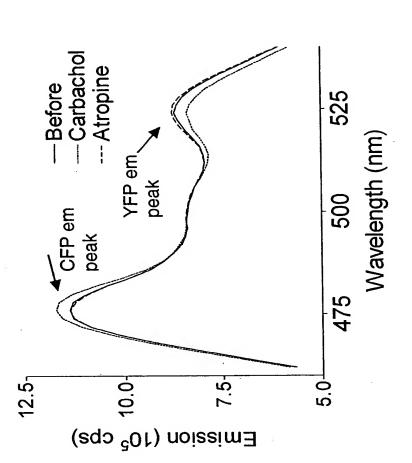
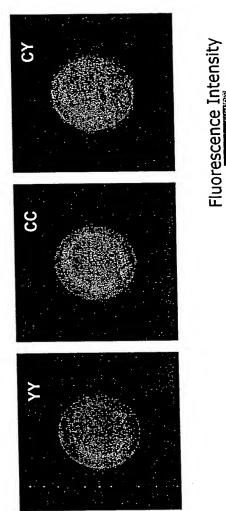


Fig. 25

made up of αo tethered to the receptor in the presence of an agonist Fluorescence spectra from insect cells containing a biosensor and antagonist



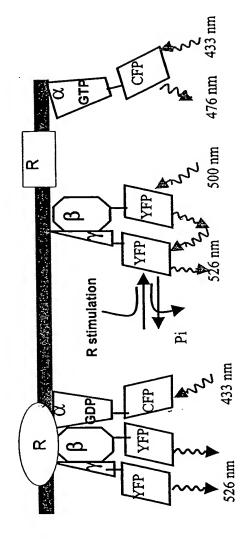
Images of Fluorescence Emission from Tethered alpha Biosensor Cells excited with Defined Spectra



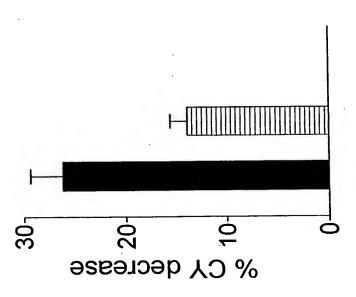
Fluorescence Intensity

Low High

Biosensor containing YFP tagged β and γ subunits



Mammalian cells containing Biosensor with two YFP molecules attached to both β and γ subunits provides stronger FRET signal change in response to agonist



Biosensor cell responds to repeated exposure to agonist and antagonist molecules with predictable changes in FRET signal intensity

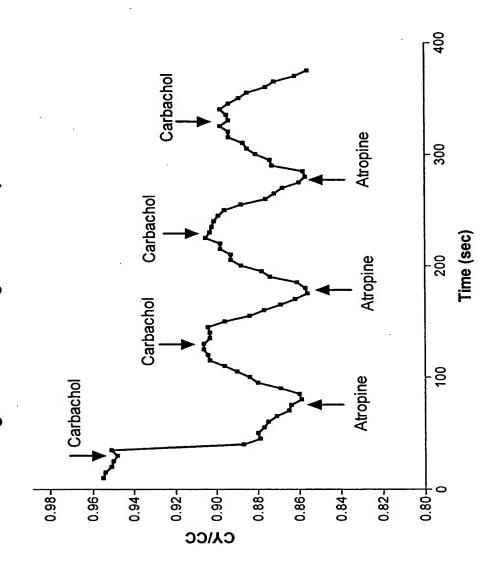


Fig. 29

Fig. 30

Go-q sensor is not activated by the M2 receptor unlike Go

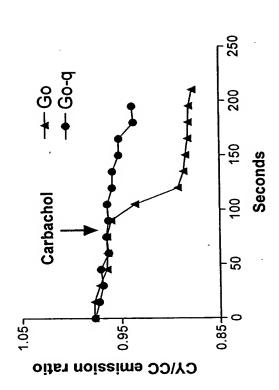


Fig. 31

Go-q sensor is activated by the M3 receptor more effectively than Go sensor

